REMARKS

The claims have been amended to obviate rejections under 35 U.S.C. § 112, paragraph 2, and certain of the rejections under 35 U.S.C. § 112, paragraph 1. Claim 48 has been amended to clarify that by the term "101P3A11 protein" is meant SEQ ID NO: 2866. In claim 48, also, "observing" has been changed to "measuring" as being more consistent with the overall claim structure. Further, claim 48 has been amended to insert the limitation of claim 56 to specify that the activity to be measured is cAMP accumulation, which in turn has downstream signaling effects. A description of these downstream signaling effects is found on page 106 of the substitute specification. As noted, it has been established in working Example 40 that the activity of 101P3A11 protein comprises an increase in cAMP accumulation (see page 106, line 38-page 107, line 6). This example further confirms, experimentally, that the effect of cyclic AMP can be exhibited in the results of further downstream signaling, one of which is phosphorylation of ERK. There is no doubt of these results as they are described in working examples. Thus, the amendments to the claims are fully supported by the specification and are made specifically in response to the rejections now outstanding. Therefore, entry of the amendment, though made after final, is respectfully requested.

The Rejections

The objection to the claim language and the rejection under 35 U.S.C. § 112, second paragraph, as well as the second part of the rejection under 35 U.S.C. § 112, first paragraph, have been overcome by amendment. It is clarified, now, that "101P3A11 protein" refers solely to SEQ ID NO: 2866, which was the intent all along. This overcomes the objection and the second portion of the rejection under 35 U.S.C. § 112, paragraph 1. The activity of the protein has also been

defined in claim 48 by inserting the limitations of claim 56 which was not included in the rejection under paragraph 2. The inclusion of downstream signaling effects is fully supported by the specification on page 107 and by existing claim 55 which has been amended merely to conform its wording to the reworded claim 48.

Accordingly, the only outstanding rejection is with respect to enablement as set forth on pages 3-5 of the Office action. This rejection was applied to all claims; as applied to claim 48, a portion of this has been overcome by defining the protein activity to which the claim refers. Accordingly, the rejection as applied to claim 48 on this basis appears moot.

As to the remainder of the rejection, this does not appear to be based on any assertion that one would not know how to measure the protein activity of 101P3A11 based on the teachings of the specification. There is no assertion that the specification fails to teach one how actually to perform the steps in the method claimed. Rather, the Office questions whether the candidate identified by the claimed method would itself be of any value – the Office states that "one would not know how to use the agents identified by the claimed method."

This is clearly not so. The specification teaches how to use the agents thus identified. At page 43, line 33, it is clearly stated that "therapeutic approaches that inhibit the activity of the 101P3A11 protein are useful for patients suffering from a cancer that expresses 101P3A11." In particular, antibodies which inhibit the activity of this protein are stated to be useful, in support specifically, of claim 54. (See page 47, beginning at line 15.) The use of antibodies as inhibitors has been demonstrated by Declaration in copending application 10/147,368 to inhibit the growth of cancers that express 101P3A11. Antibodies to this protein are shown to inhibit the growth of human prostate cancer xenographs in mice. A copy of the declaration submitted in that case along with the experimental results is enclosed. Applicants wish to make clear that these antibodies are to

the same protein as that of the present claims. The relevant sequence in 10/147,368 is SEQ ID NO: 28. This is identical to SEQ ID NO: 2866 in the present application except that SEQ ID NO: 2866 shows an extra methionine at the N-terminus which behaves as a possible superfluous start codon, so that SEQ ID NO: 2866 has 318 amino acids. The 101P3A11 protein itself has 317 amino acids and is lacking the extra N-terminal methionine, as noted on page 6 of the substitute specification which states that Figure 3 shows the amino acid sequence of 101P3A11 and that this protein has 317 amino acids. That figure is, however, referenced to SEQ ID NO: 2866. If necessary, a substitute sequence listing can be submitted showing 101P3A11 protein as having 317 amino acids. In any event, it is not relevant for purposes of the present claims since the activity of the protein will be the same regardless of the presence or absence of this N-terminal methionine.

In summary, the declaration submitted in application 10/147,368 refers to the ability of antibodies directed against the same protein as that whose activity is to be measured according to the present claims to inhibit tumor growth.

It appears that the rejection is simply based on doubts that the method, which itself is clearly enabled, would identify substances that are successful in treating cancers that express 101P3A11. It will be noted that the claims do not require such success, they are simply directed to a method to identify an agent that decreases this protein activity which may or may not turn out to be successful in treating cancers. This is no different from any screening assay; screening assays are extremely useful in identifying compounds that are candidates for treatment; only a small fraction of these candidates turn out to be viable therapeutics. This does not render the screening methods useless; if they were useless, pharmaceutical companies would not spend millions of dollars annually to conduct them, and there would be no way to select a small number of compounds for further testing.

The Office cites some papers showing problems that might affect the predictive value of the assay. The first paper cited, Chang, *et al., Leukemia* (2003) 17:1263-1293, actually supports the position taken by applicants. The paper states, as the Office says it does, that the signaling pathway which ends with ERK mediates transcription. The fact that the manner of mediation is not completely understood, or that this particular pathway may not be the only one relevant to cancers, does not destroy the utility of the assay. Instead, this paper takes the assertions of applicants one step further toward verification of utility.

The Office then cites Hummler, E., *et al., PNAS* (1994) 91:5647-5661. This paper indicates that signaling systems are complex and interrelated and that there is not a linear relationship between cAMP and transcriptional regulation. Why this is relevant to the present claims is unclear. Applicants are well aware that regulation of transcription is complex and that the ability of a candidate compound to inhibit cAMP accumulation mediated by 101P3A11 does not have a disclosed linear pathway to inhibition of cancer growth. However, this is irrelevant to the utility of the method of the invention. As stated by the Court in *Fromson v. Advance Offset Plate, Inc.*, 720 F2d 1565, 219 USPQ 1137 (Fed. Cir. 1983), "It is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests" citing *Diamond Rubber Co. v. Consolidated Rubber Tire Co.*, 220 US 428 (S.Ct. 1911).

Thus, it is quite clear that applicants need not describe the exact mechanisms whereby inhibition of the activity of 101P3A11 protein might result in the inhibition of cancer growth.

Also cited by the Office is Xu, *et al., FASEB J.* (2001) 15:A313 for the proposition that there are regulatory systems which might overcome perturbations imposed on a system. Again, this is common knowledge and, applicants believe, irrelevant to the invention which rests on the concept that high levels of 101P3A11 protein are found in cancers and that this protein has a defined activity

which can be measured. It stands to reason that if the protein is at high levels in cancer, its activity is probably contributing to the growth of the cancer and therefore inhibition of this activity should inhibit cancer growth. This is not a proposition contrary to general scientific principles.

Respectfully, the Office appears to require a level of certainty with respect to efficacy that is not required by the law. Perhaps relevant to this issue is the decision in *Moleculon Research Corp. v. CBS, Inc.*, 793 F2d 1261, 229 USPQ 805 (Fed. Cir. 1986) where claims to a method of solving a Rubik's Cube puzzle were asserted to be un-useful because they do not teach the complicated method of solving it. As stated by the Court, the claims were directed to a method for restoring a preselected pattern using a general approach for solving the puzzle. The Court stated that neither the claims nor the disclosure need set forth a particular series of moves to solve the puzzle as these moves depend on how the preselected pattern was randomized and there may be more than one sequence of steps. All the claims needed to do, apparently, was to claim an approach.

Further, as stated by the Court in *Envirotech Corp. v. Al George, Inc.*, 730 F2d 753, 221 USPQ 473 (Fed. Cir. 1984), the fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility citing *Raytheon Co. v. Roper Corp.*, 724 F2d 951, 220 USPQ 592 (Fed. Cir. 1983) among other cases. As stated, only some degree of utility is sufficient for patentability citing *E.I. DuPont de Nemours v. Berkley and Co.*, 620 F2d 1247, 205 USPQ 1 (8th Cir. 1980). "The defense of non-utility cannot be sustained without proof of total incapacity."

Total incapacity is far from the case here. Data are supplied which demonstrate that the activity of the 101P3A11 protein is elevated in cells that express it and that cells that express this protein characterize various cancer cells. This appears sufficient basis to assert the utility of the claimed method which is designed to provide useful candidates for cancer therapy.

For these reasons, the rejection for lack of enablement may clearly be withdrawn.

Conclusion

There is no assertion that the specification does not enable one to practice the invention as claimed, although the rejection is stated in those terms. The rejection appears based entirely on the assertion that by performing the method of the invention the compounds identified as successful inhibitors would not be useful. This is contrary to the teachings of the specification which demonstrate that such inhibitors are good candidates as anticancer drugs. This is further supported by the enclosed declaration copy from copending application 10/147,368 which demonstrates that antibodies to this protein do indeed inhibit cancer growth. Accordingly, it is believed that claims 48, 50 and 54-55 are in a position for allowance and passage of these claims to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 511582002420.

Respectfully submitted,

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